FIG. 1

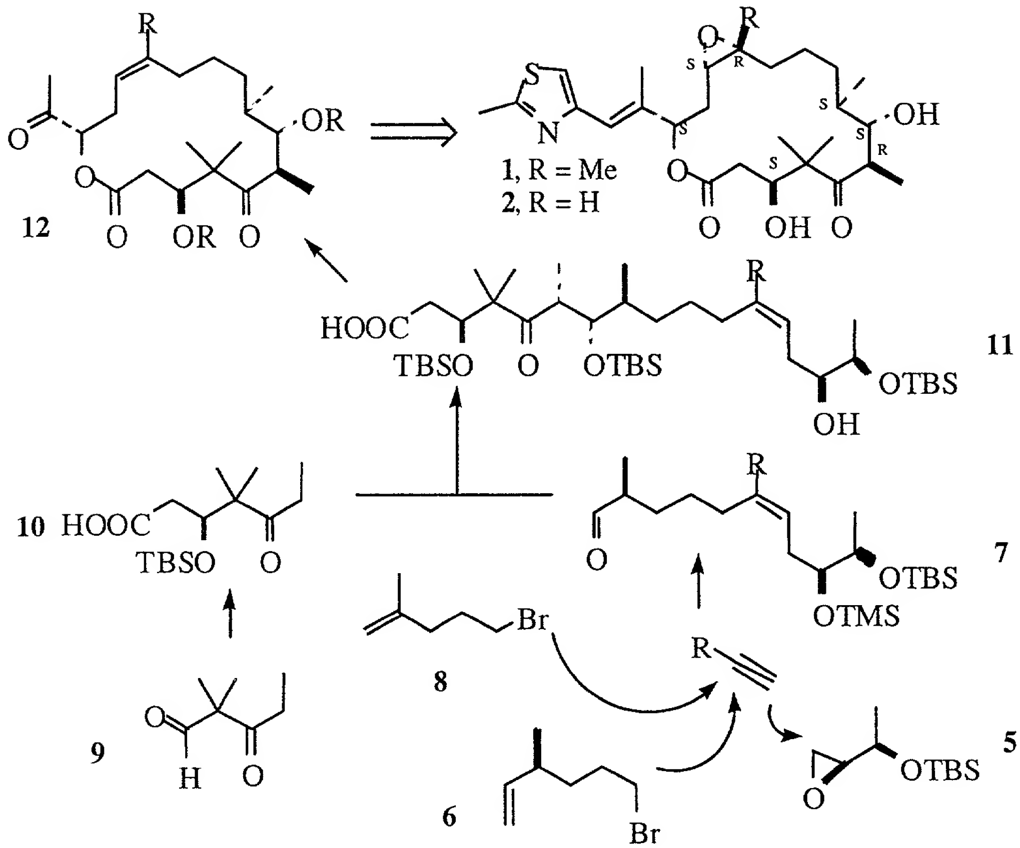

1, R = Me
2, R = H
12
11
10
7
8
9
6
5
HOOC
TBSO
OTBS
OTMS
OH
OR
Br

FIG.2

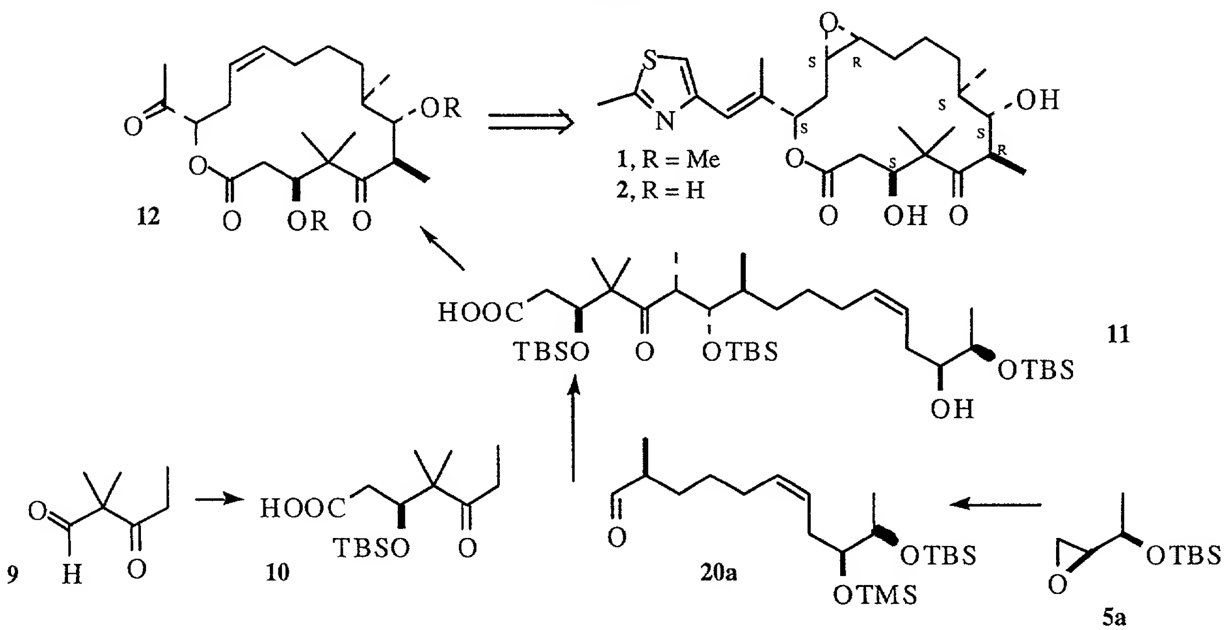
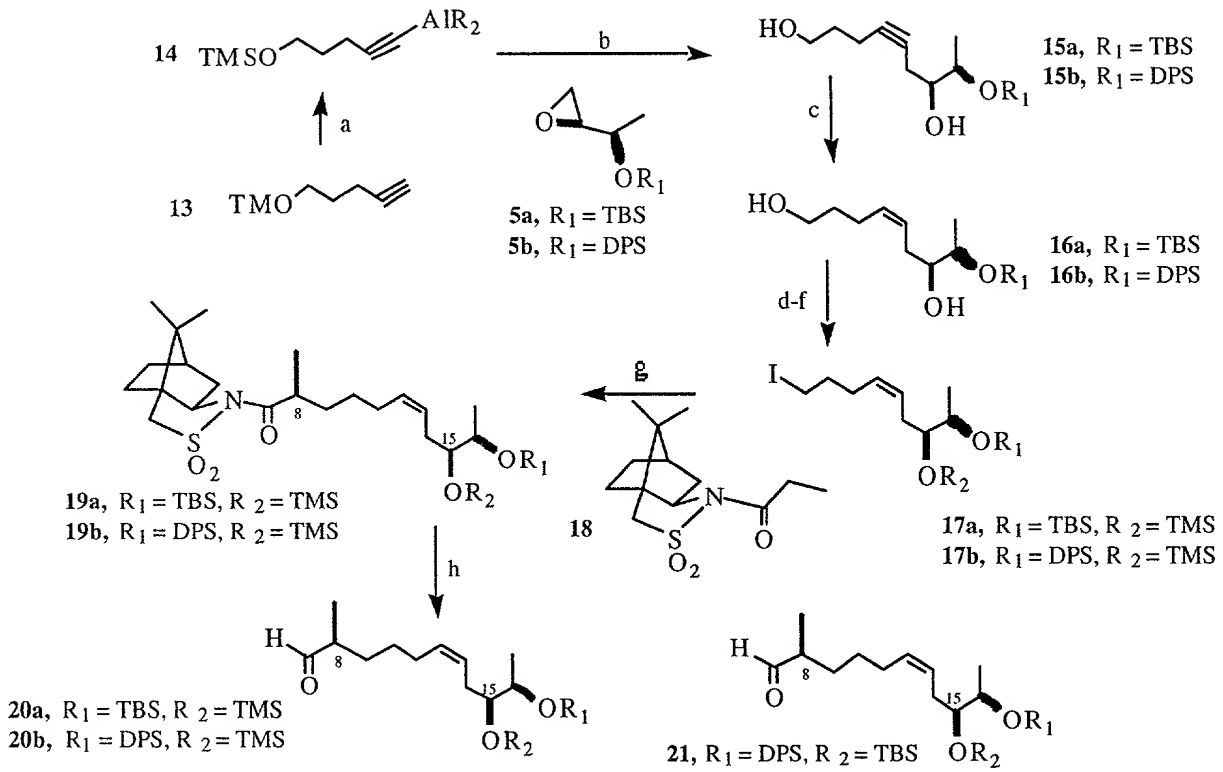
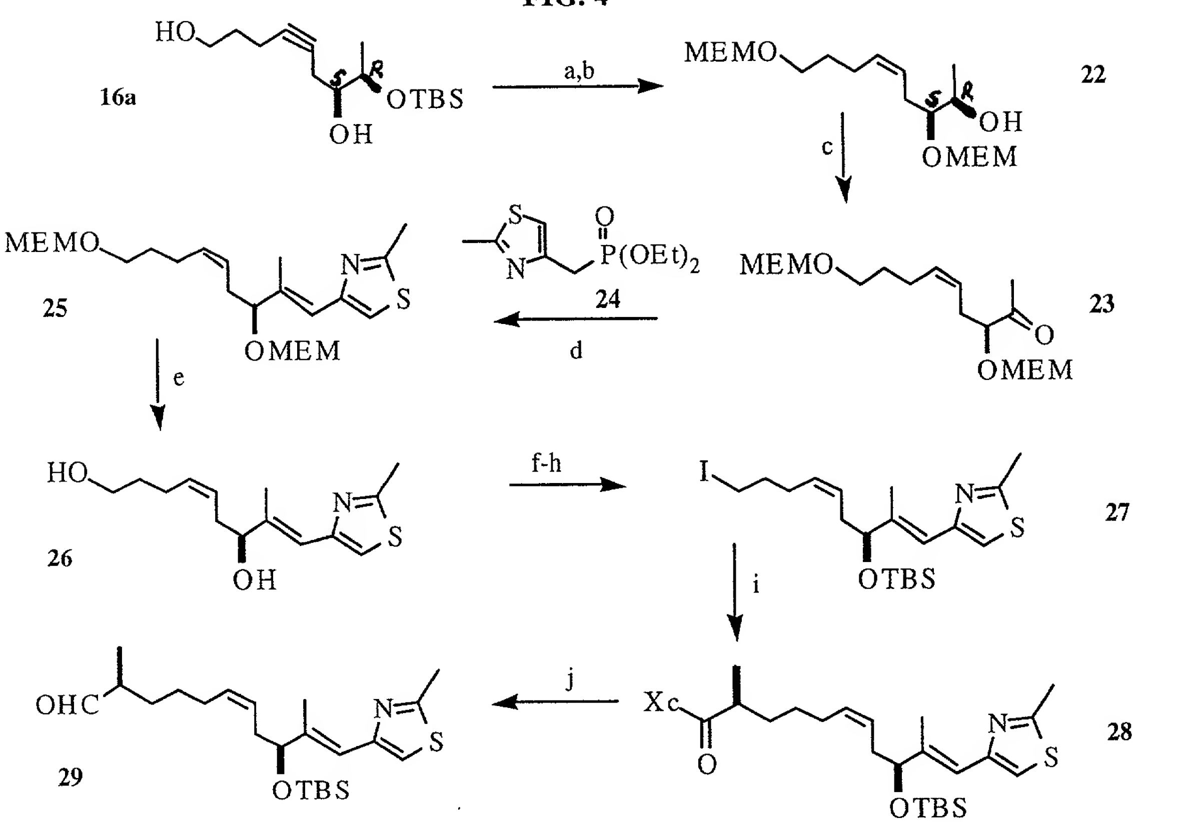

1, R = Me
2, R = H
12
11
9
10
20a
5a
HOOC
TBSO
OTBS
OTMS
OH
OR

FIG. 3



Key: a) n-BuLi, Ether; Et_2AlCl, toluene; b) **5** then dil.HCl; c) Lindelar Catalyst, H_2; d) TsCl, THF, pyridine; e) TMStriflate, CH_2Cl_2, 2,6-Lutidine; f) NaI, acetone, Δ; g) N-Propionylcamphorsultam **18**, n-BuLi, then **17**; h) DIBAH, THF-CH_2Cl_2.

FIG. 4



Key: a) MEMCl, DIPA, CH_2Cl_2; b) TBAF, THF; c) Swern Oxidation; d) Horner-Emmons Reaction, LDA, THF, **24**; then ketone **23**; e) HCl, H_2O, THF; f) TsCl, pyridine, CH_2Cl_2; g) TBSOTf, DIPA; h) NaI, acetone, Δ; i) N-propionylcamphorsultam **18**, n-BuLi, then iodide; j) DIBAH, CH_2Cl_2.

FIG. 5

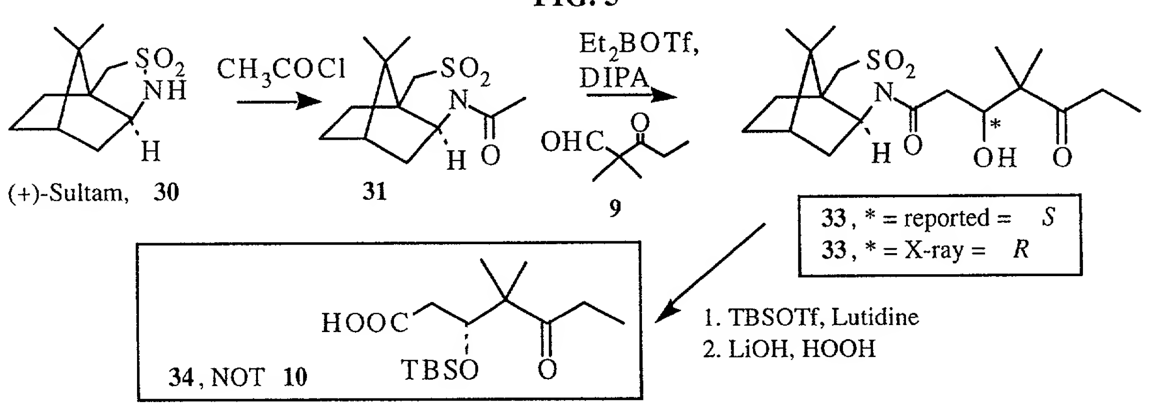


FIG. 5a

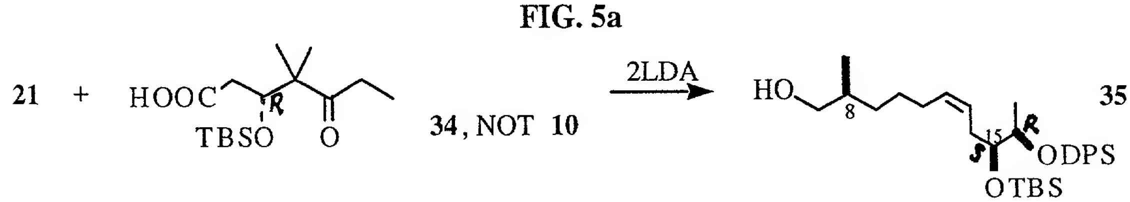


FIG. 6

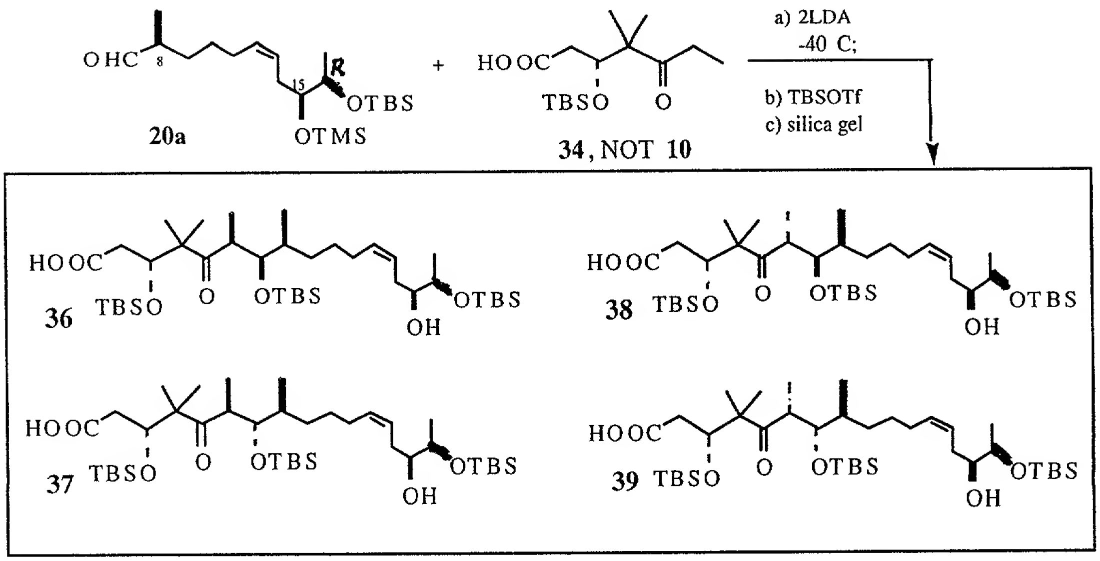
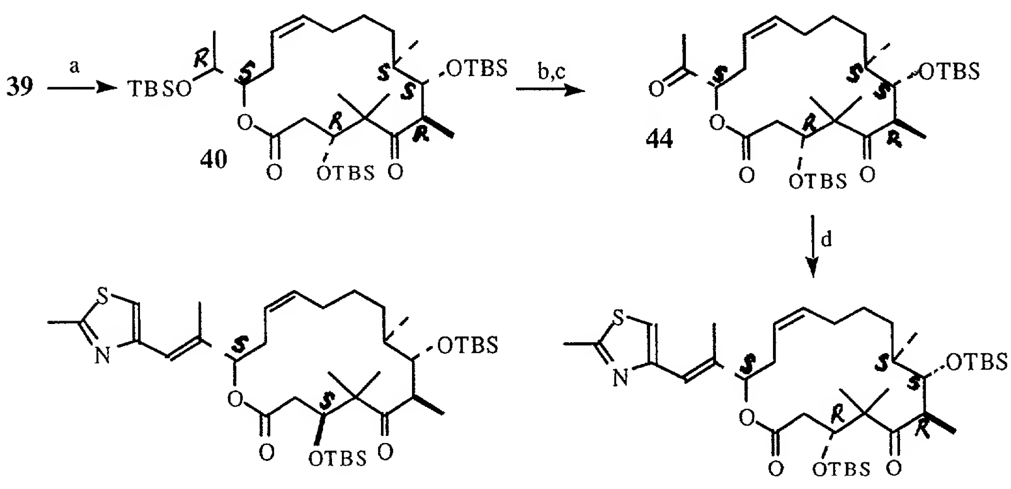


FIG. 7



46, Nicolaou

45, matched Danishevsky's epimer.

Key: a) $Cl_3C_6H_2COCl$, pyridine, DMAP; b) TBAF, THF; c) PCC, CH_2Cl_2; d) Horner-Emmons: LDA, **24**.

FIG. 8

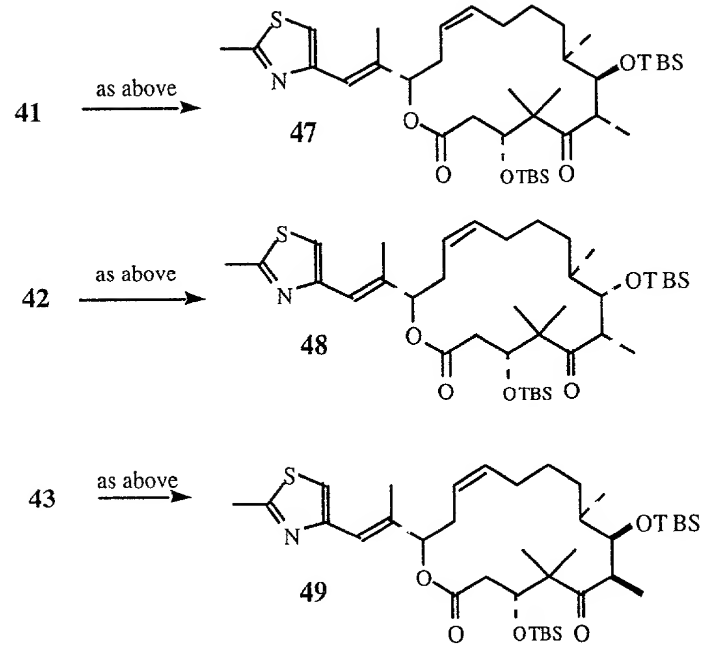

41
as above
47
OTBS
OTBS
42
as above
48
43
as above
49
S
N
O

FIG. 9

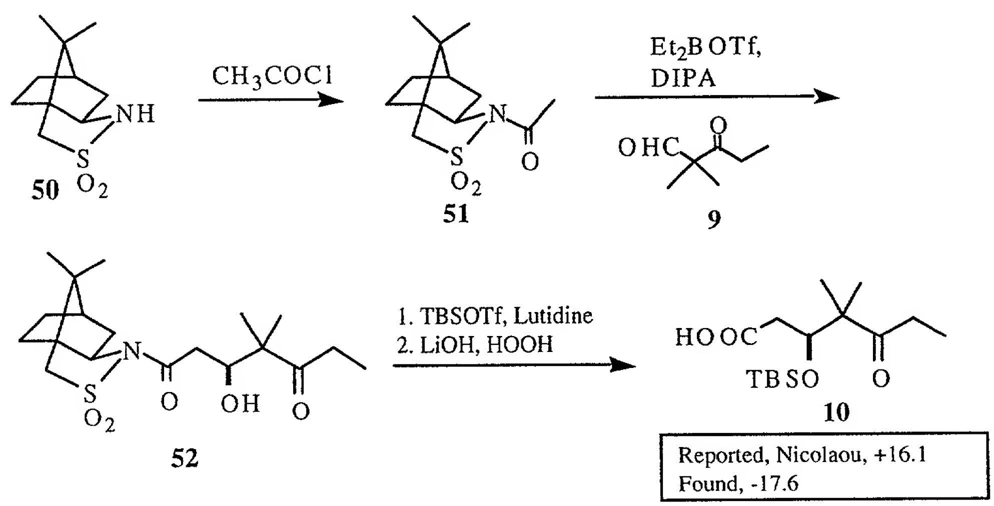

NH
50
O_2
CH_3COCl
51
Et_2BOTf,
DIPA
OHC
9
52
OH
1. TBSOTf, Lutidine
2. LiOH, HOOH
HOOC
TBSO
10
Reported, Nicolaou, +16.1
Found, -17.6

FIG. 10

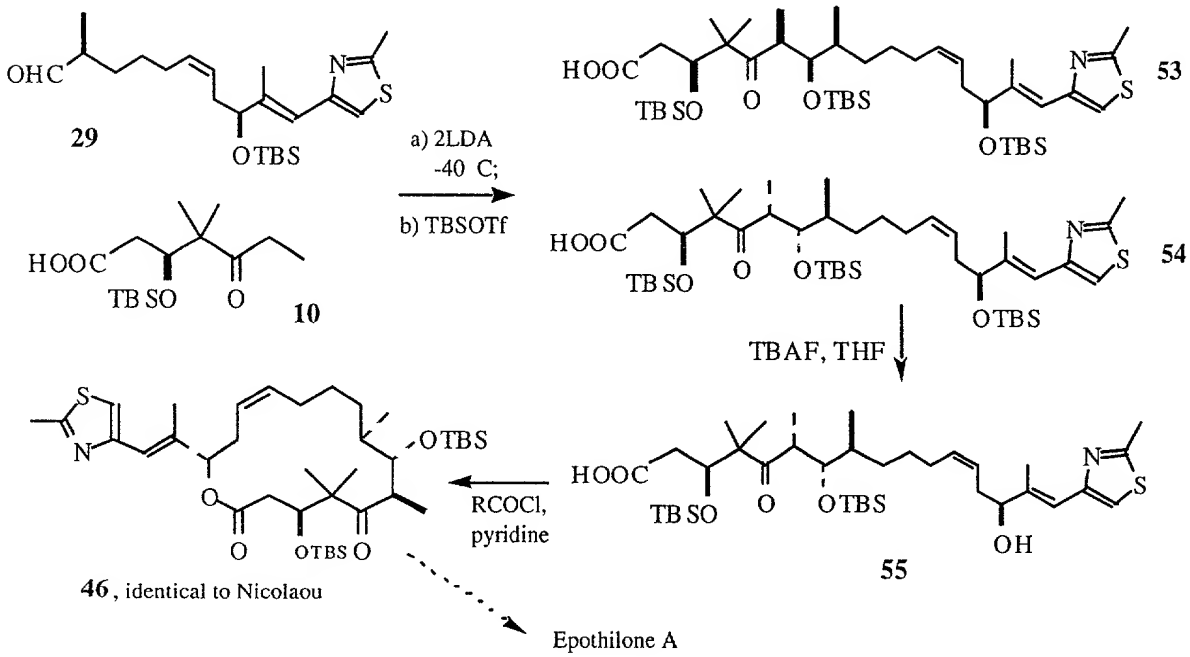
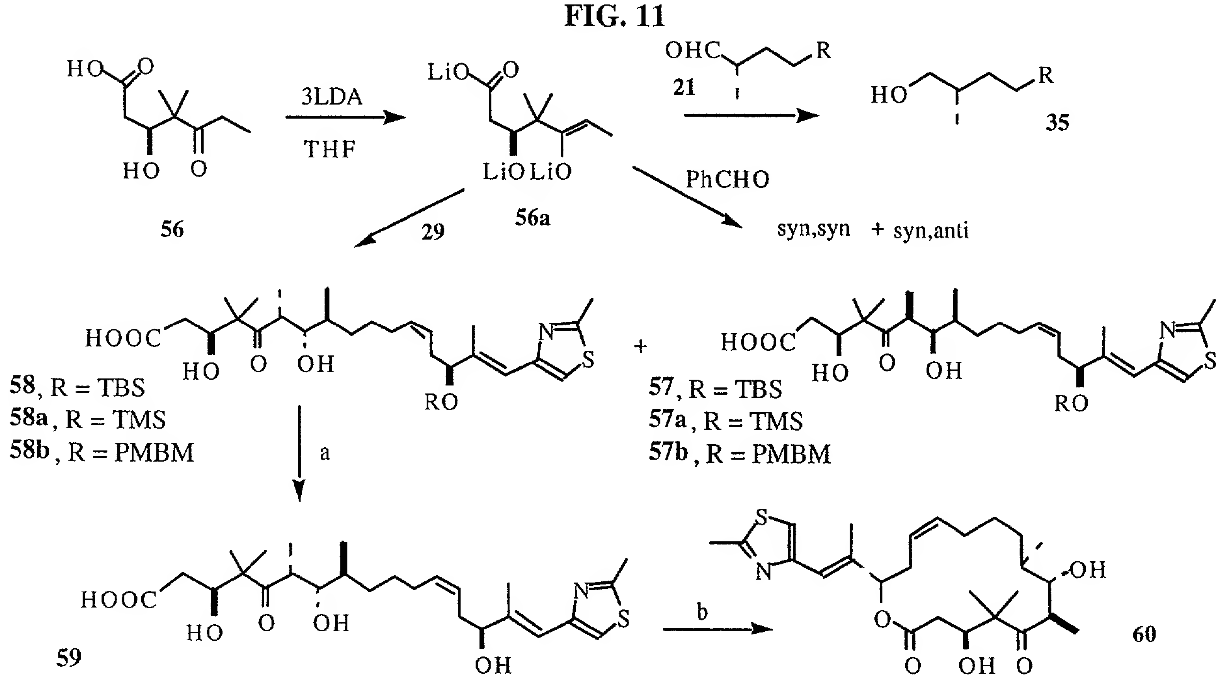


FIG. 11



Key: a) **58**, TBAF, THF; **58a**, chromatography; **58b**, dil. acid or DDQ, CH_2Cl_2, water; b) PhSO2Cl, pyridine, or $Cl_3PhCOCl$, pyridine, DMAP, CH_2Cl_2.

FIG. 12

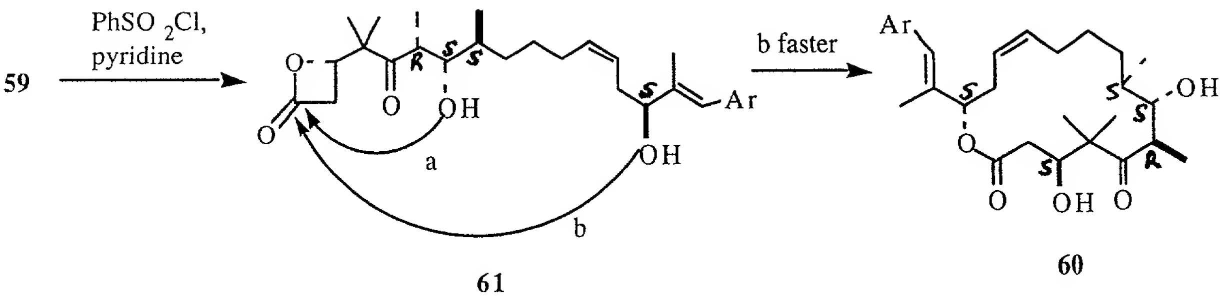
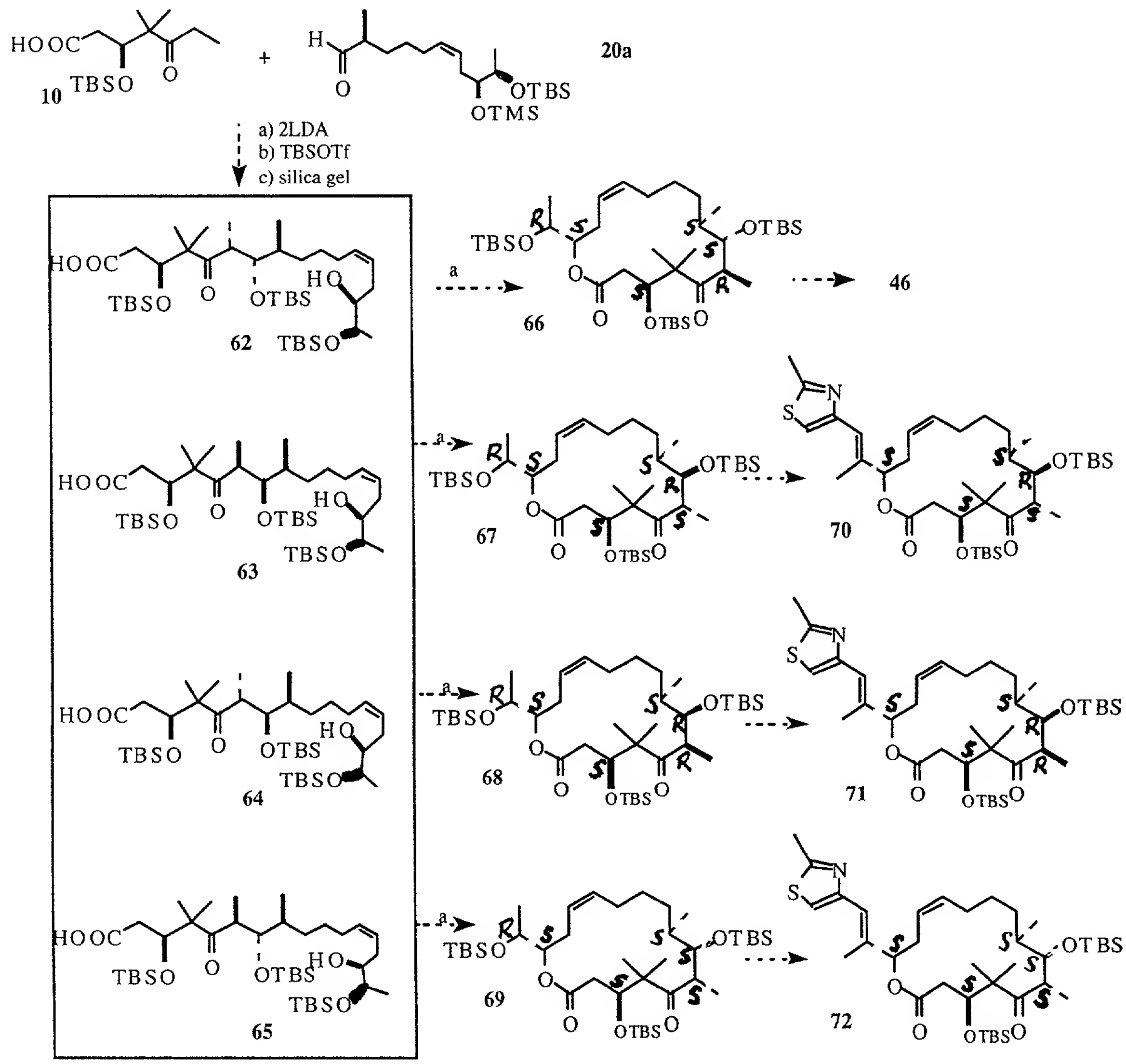
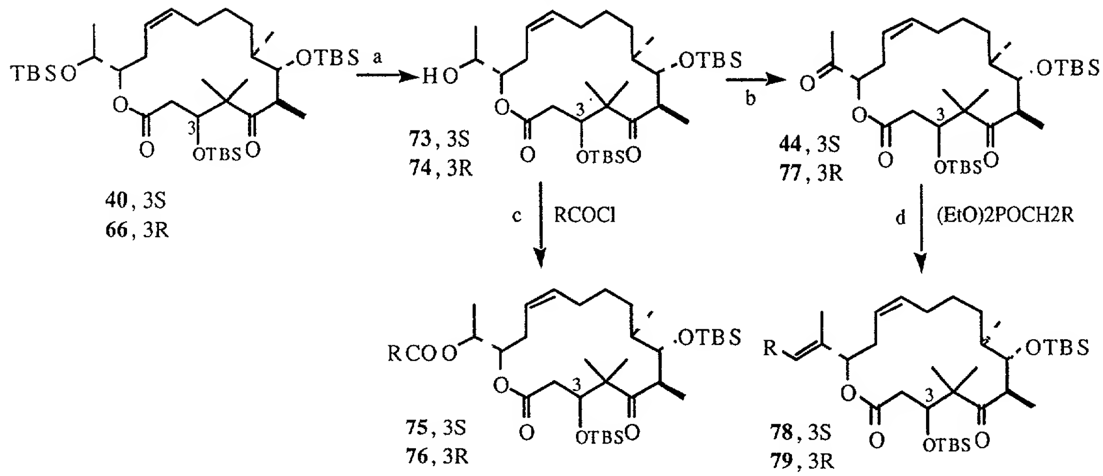


FIG. 13



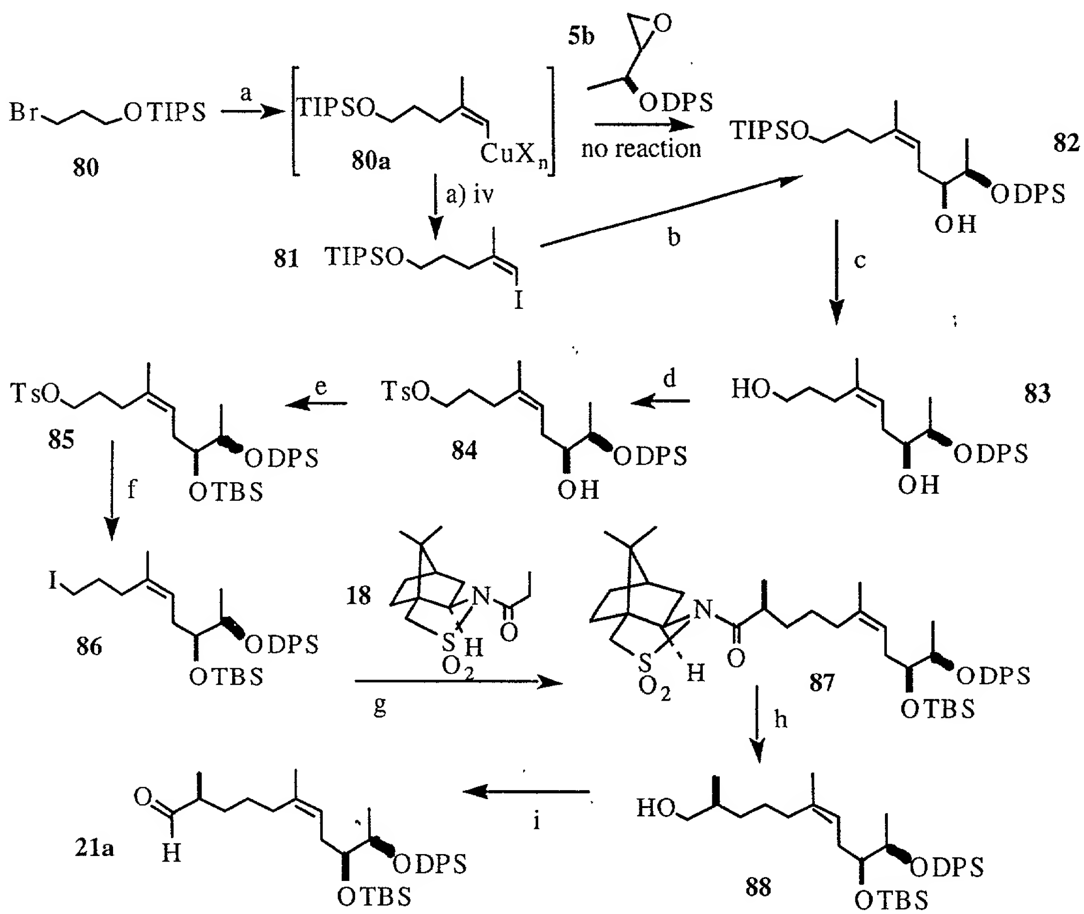
Key: a) as in Figure 7

FIG. 14



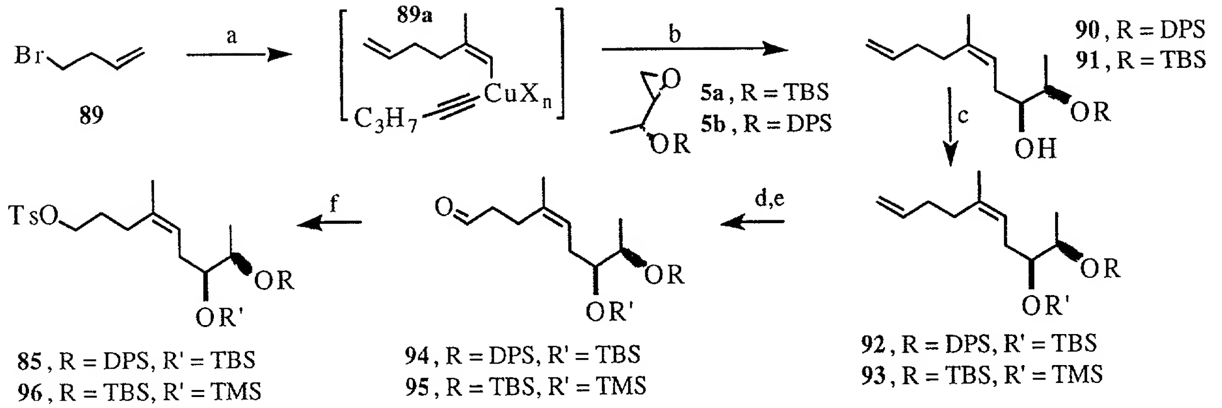
Key: a) 1.0 TBAF, THF; b) PCC, CH_2Cl_2; c) pyridine or DMAP, CH_2Cl_2; d) Horner-Emmons: LDA, **24** or other phosphonates.

FIG. 15



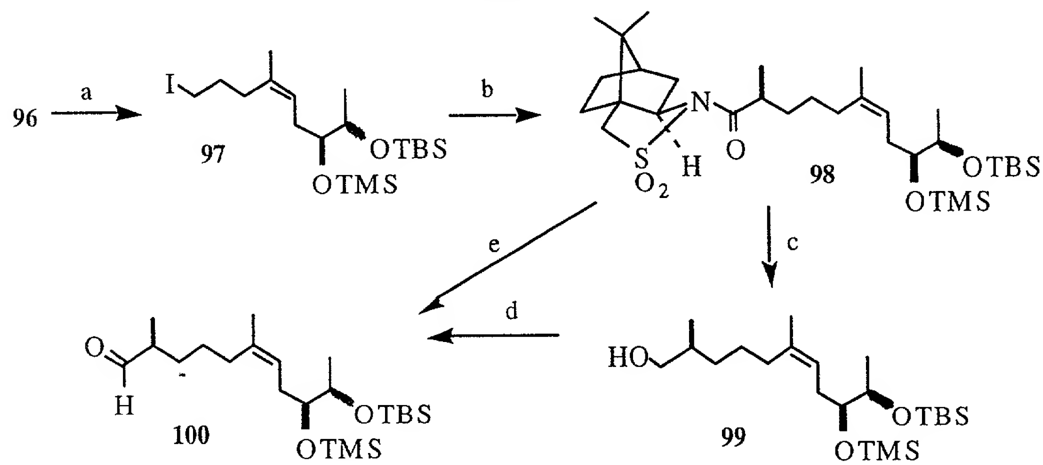
Key: a] i)Mg, ether; ii) CuBr•DMS; iii) propyne; iv) I_2; b] i) n-BuLi; ii) Me_2AlCl; iii) **5b**; c) HCl, EtOH; d) TsCl, pyridine; e) TBSOTf, 2,6-lutidine, CH_2Cl_2; f) NaI, acetone; g) **18**, n-BuLi, -40 °C, THF; h) $LiAlH_4$, THF; d) pyridine•SO_3, CH_2Cl_2; Et_3N.

FIG. 16



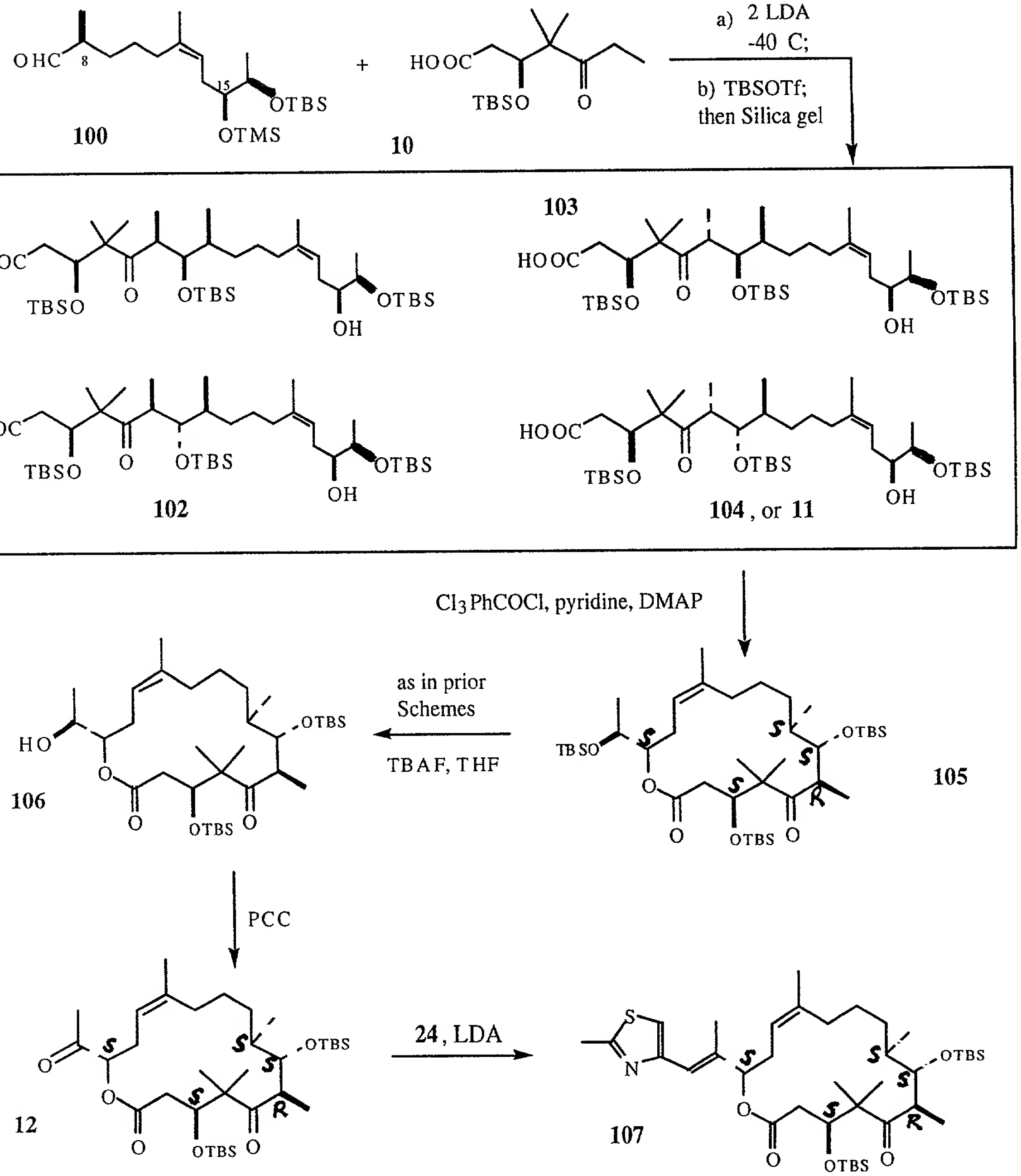
Key: a] i) Mg, ether; ii) CuBr•DMS, DMS, ether; iii) propyne; iv) pentynyl lithium; b) **5b**, -40 °C, 36 hrs; c) TBSOTf, 2,6-lutidine, CH_2Cl_2; d) AD-mix a, e) $NaIO_4$, EtOH, HOH; f) $NaBH_4$, MeOH; g) TsCl, pyridine.

FIG. 17



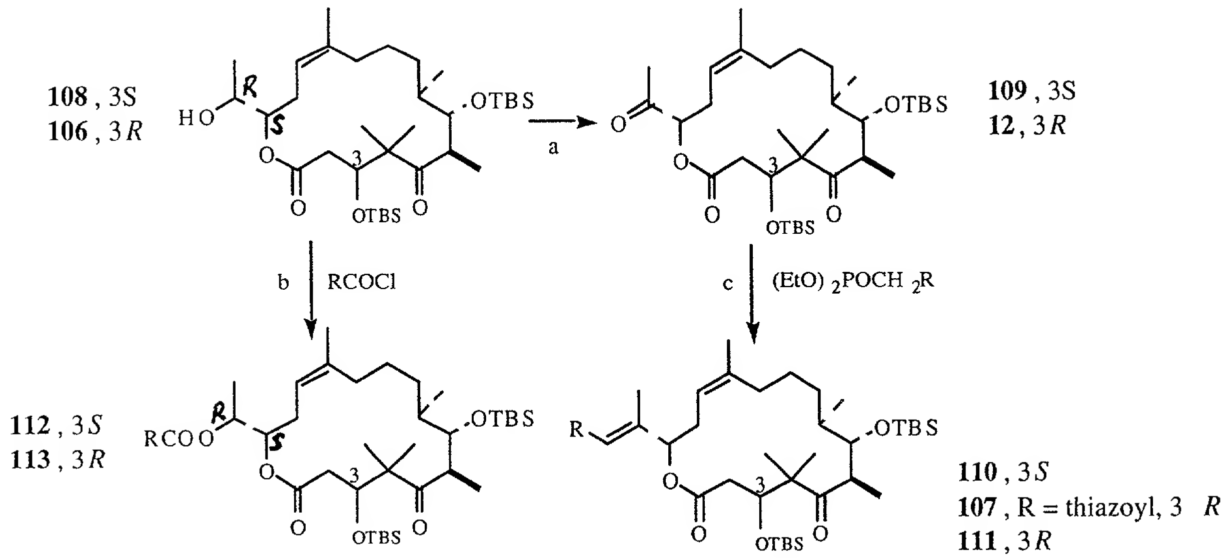
Key: a) NaI, acetone; b) **18**, n-BuLi, -40 _C, THF; c) $LiAlH_4$, THF; d) pyridine•SO_3, CH_2Cl_2; Et_3N; e) DIBAH, ether, -78 °C.

FIG. 18



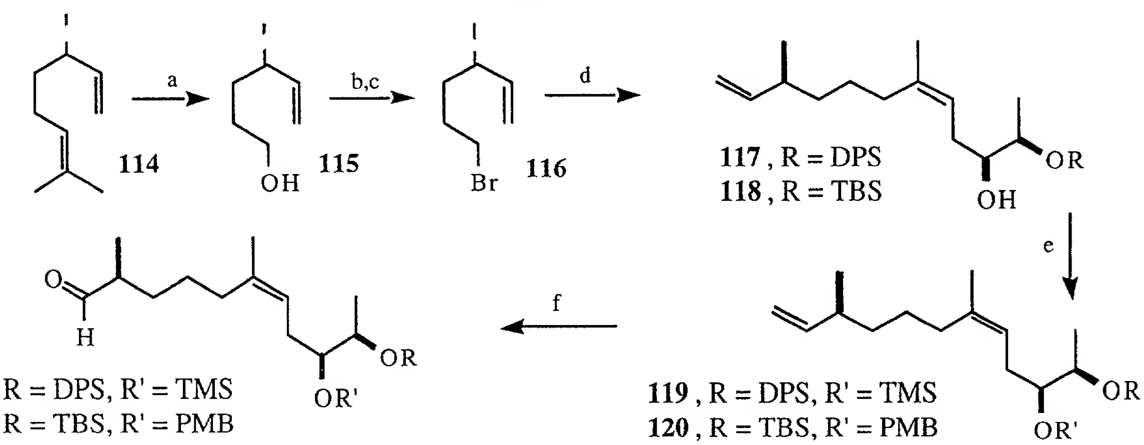
OHC
8
15
OTBS
OTMS
100
+
HOOC
TBSO
O
10
a) 2 LDA
-40 C;
b) TBSOTf;
then Silica gel
101
HOOC
TBSO
O
OTBS
OTBS
OH
103
HOOC
TBSO
O
OTBS
OTBS
OH
102
104, or 11
Cl3 PhCOCl, pyridine, DMAP
105
as in prior
Schemes
TBAF, THF
106
HO
PCC
12
24, LDA
107

FIG. 19



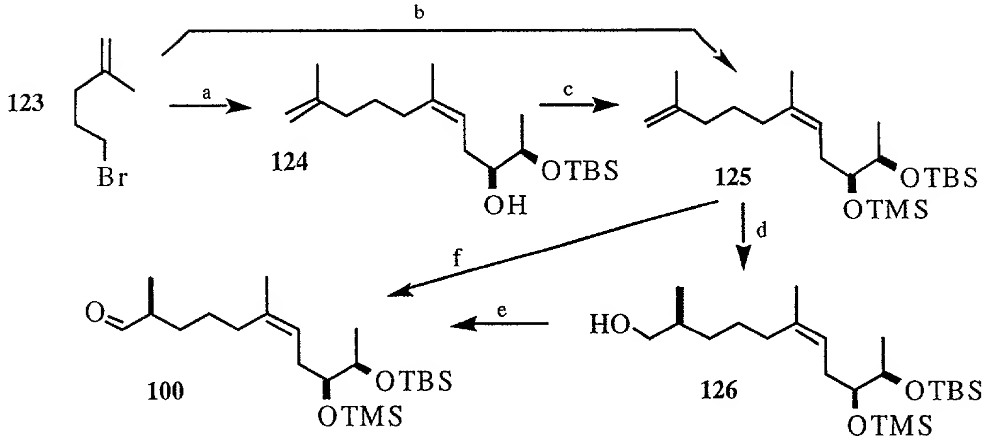
Key: a) PCC, CH_2Cl_2; b) pyridine or DMAP, CH_2Cl_2; c) Horner-Emmons: LDA, **24** or other phosphonates.

FIG. 20



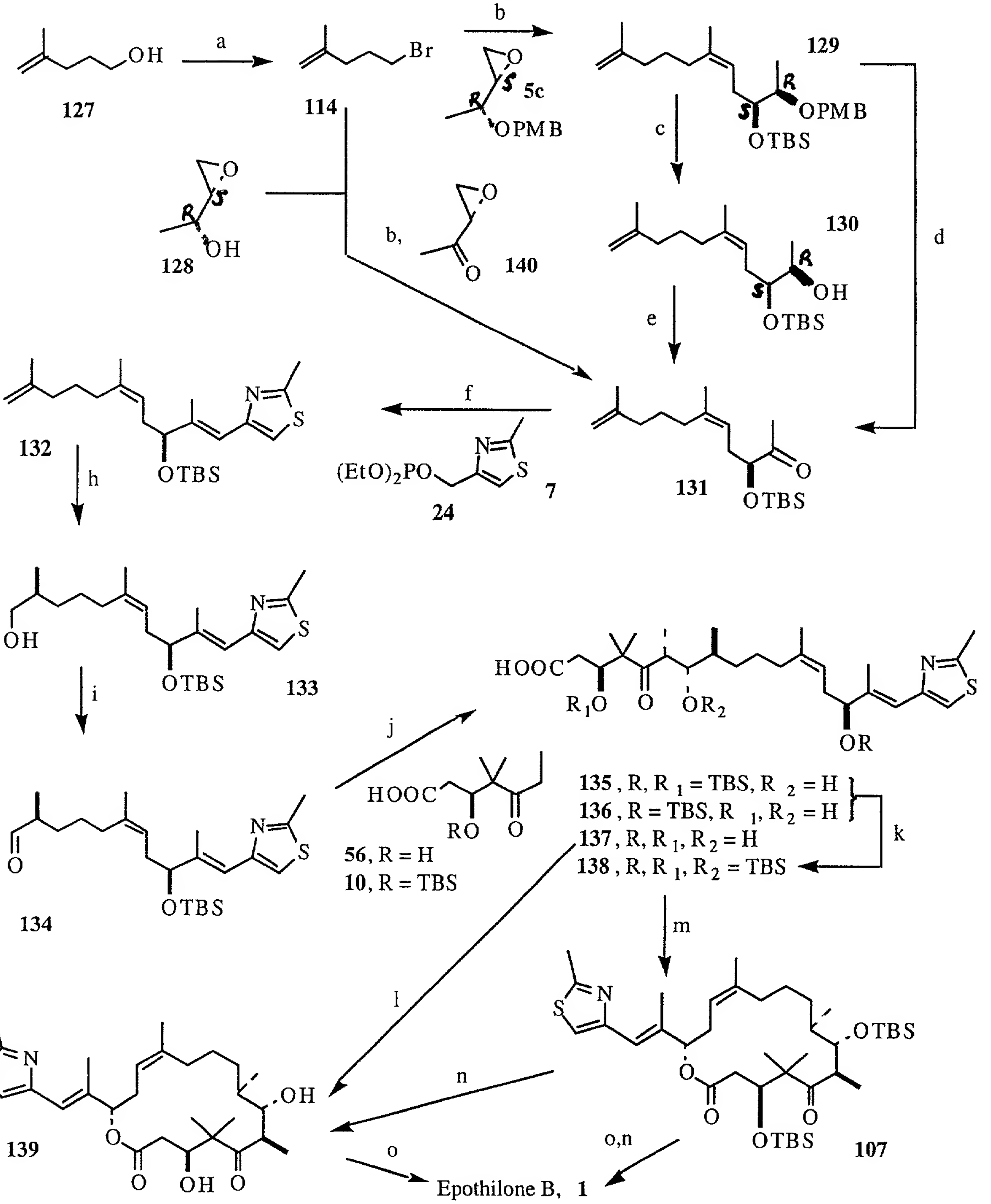
Key: a) O_3, MeOH, -78 _C; then $NaBH_4$; b) TsCl, pyridine; c) LiBr, acetone; d] i) Mg, ether; ii) CuBr•DMS, DMS, ether; iii) propyne; iv) pentynyl lithium; v) **5a** or **5b**, -40 °C, 36 hrs; e) TMSOTf, 2,6-lutidine, CH_2Cl_2; or p-$MeOC_6H_4CH_2Br$, NaH, DMF; f) ADmix a; then $NaIO_4$.

FIG. 21



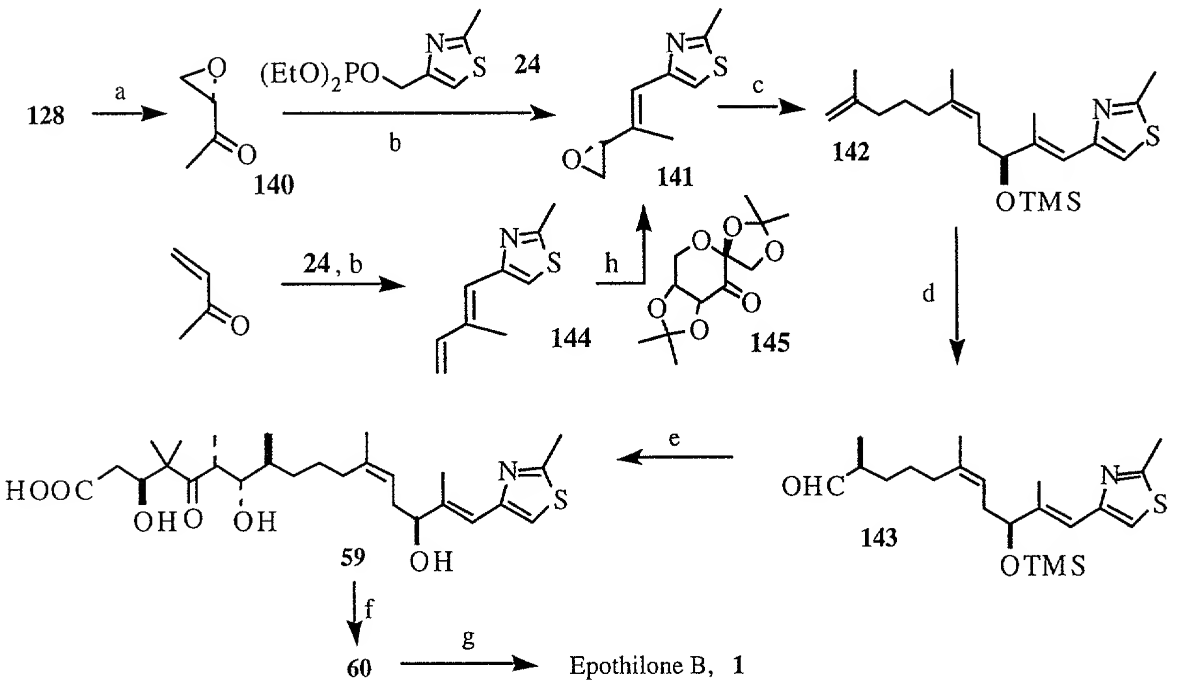
Key: a] i) Mg, ether; ii) CuBr•DMS, DMS, ether; iii) propyne; iv) pentynyl lithium; v) **5a**, -40 °C, 36 hrs; b] i) Mg, ether; ii) CuBr•DMS, DMS, ether; iii) propyne; iv) pentynyl lithium; v) **5a**, -40 _C, 36 hrs; vi) TMSOTf, -78 °C; c) TMSOTf, 2,6-lutidine, CH_2Cl_2; d) (ipc)2BH, THF, -20 °C; then H_2O_2, NaOH; e) pyr•SO_3, DMSO, Et_3N, CH_2Cl_2; f) (ipc)2BH, THF, -20 °C; then PCC, CH_2Cl_2.

FIG. 22



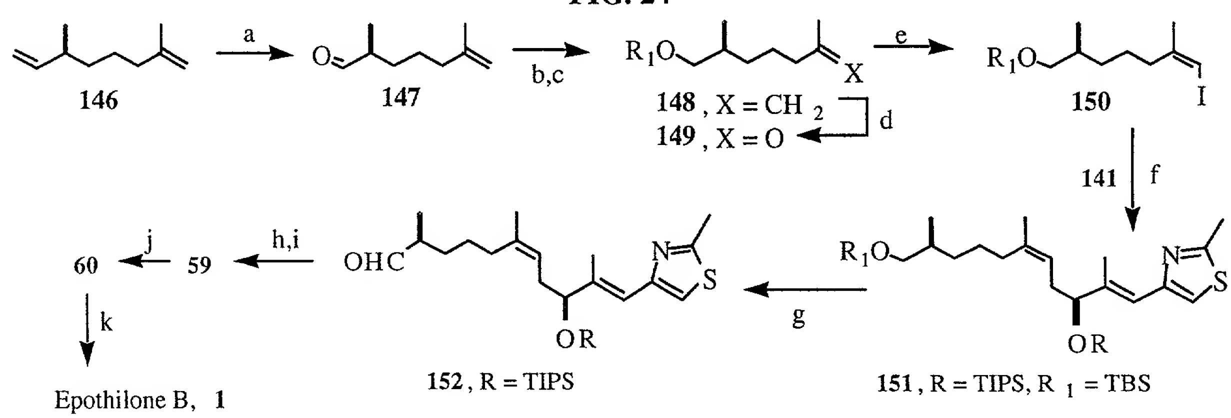
Key: a) PBr_3; b) Mg, ether; then propyne, Cu(I); pentynyl lithium; then epoxide **4**; then TBSCl; c) DDQ; d) Jones Oxidation; e) Swern Oxidation; f) Horner-Emmons reaction with **7**; g) $(Ipc)_2BH$, THF; then PCC; h) $(Ipc)_2BH$, THF; then HOONa; i) Pyridine•SO_3, Et_3N, CH_2Cl_2; j) slight excess LDA, THF, -40 °C; k) TBSOTf, 2,6-lutidine, CH_2Cl_2; l) $PhSO_2Cl$, pyridine; m) $Cl_3C_6H_2COCl$, pyridine, DMAP; n) TBAF, THF; o) Dimethyldioxirane, acetone.

FIG. 23



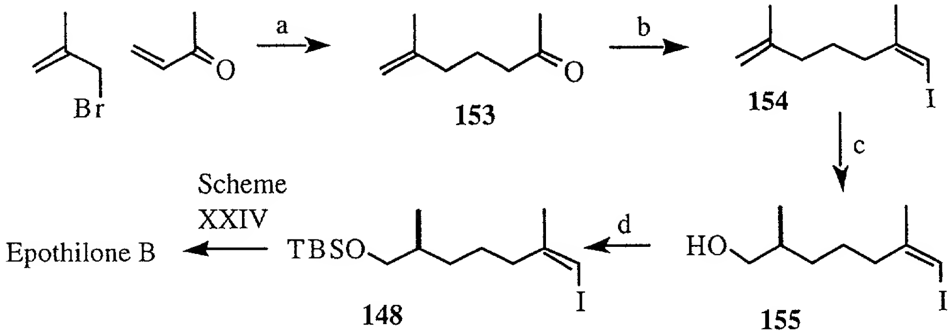
Key: a) Cr(VI), or pyridine•SO_3, DMSO, Et_3N, CH_2Cl_2; b) LDA, **24**, then **140**; c] i) **123**, Mg, ether; ii) CuBr•DMS, DMS, ether; iii) propyne; iv) pentynyl lithium; v) **141**, -40 °C, 36 hrs; vi) TMSOTf, -78 °C; d) $(ipc)_2BH$; then Cr(VI); e) **56a**, THF, -78 °C; then silica gel; f) $PhSO_2Cl$, pyridine, CH_2Cl_2; g) dimethyldioxirane, acetone; h) chiral ketone **145**, oxone, pH 7-8, aq. CH_3CN (Y. Shi, et al., J. Org. Chem., 63(23), 8475 (1998).).

FIG. 24



Key: a) AD-mix; then $NaIO_4$; b) $NaBH_4$, MeOH; c) TBSCl, pyridine, CH_2Cl_2; d) O_3, CH_2Cl_2; Me_2S; e) Ph_3P=CH-I, THF; f) *t*-BuLi, then Et_2AlCl, then **141**, then TIPSCl; g) Quinolinium fluorochromate, CH_2Cl_2; h) **56a**, THF, -78 °C; i) HF•pyr, CH3CN; j) $PhSO_2Cl$, pyridine, CH_2Cl_2; k) dimethyldioxirane, acetone.

FIG. 25



Key: a) Zn/Cu, sonochem; b) Ph_3P=CH-I, THF; c) $(Ipc)_2BH$; then $NaBO_3$; d) TBSCl, pyr, CH_2Cl_2.

FIG. 26a

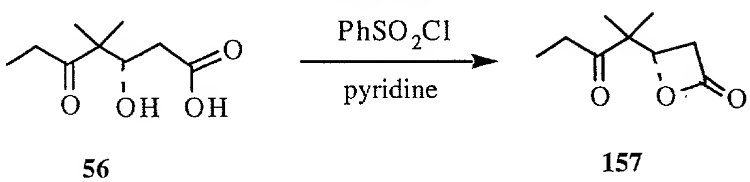
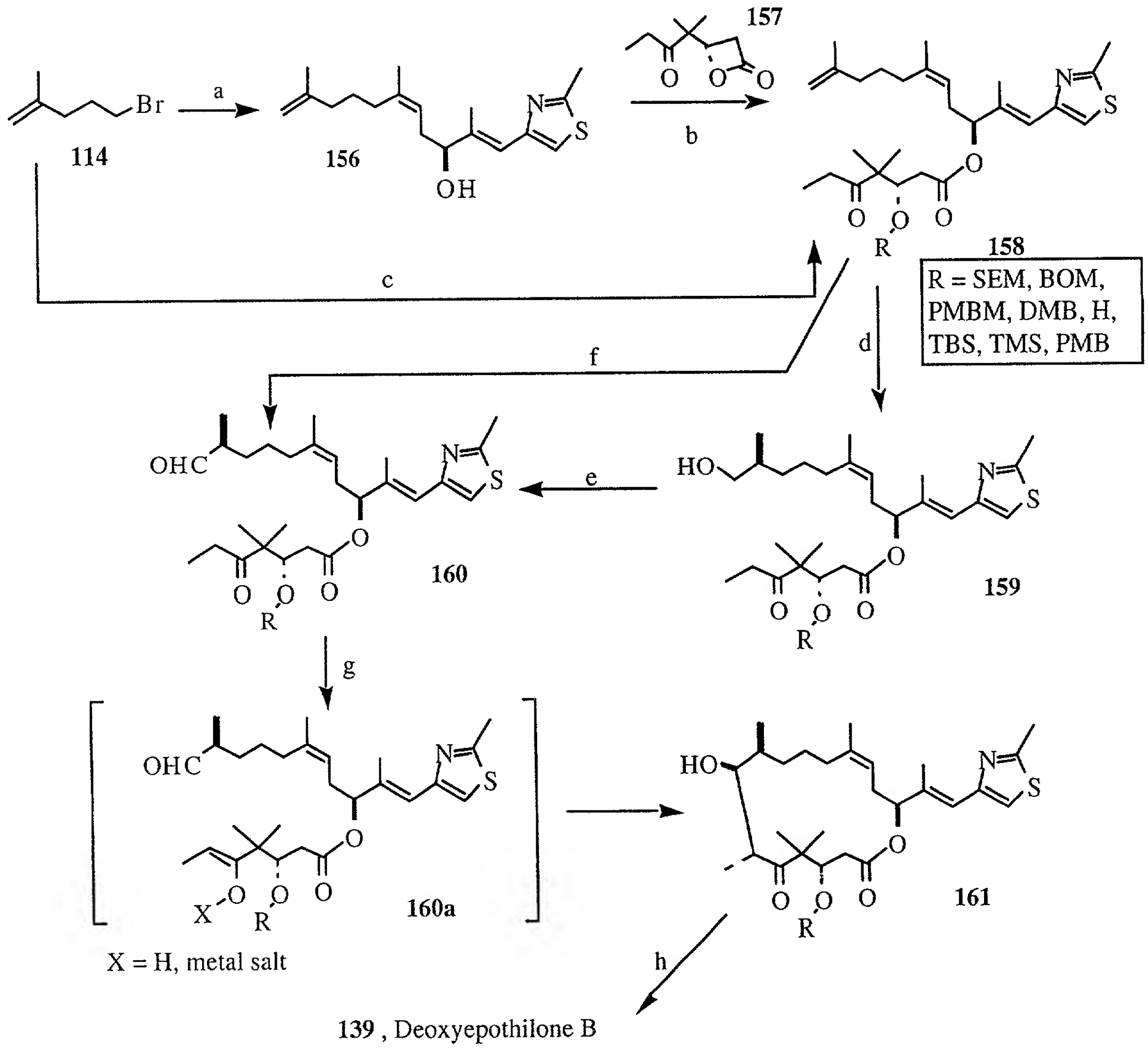
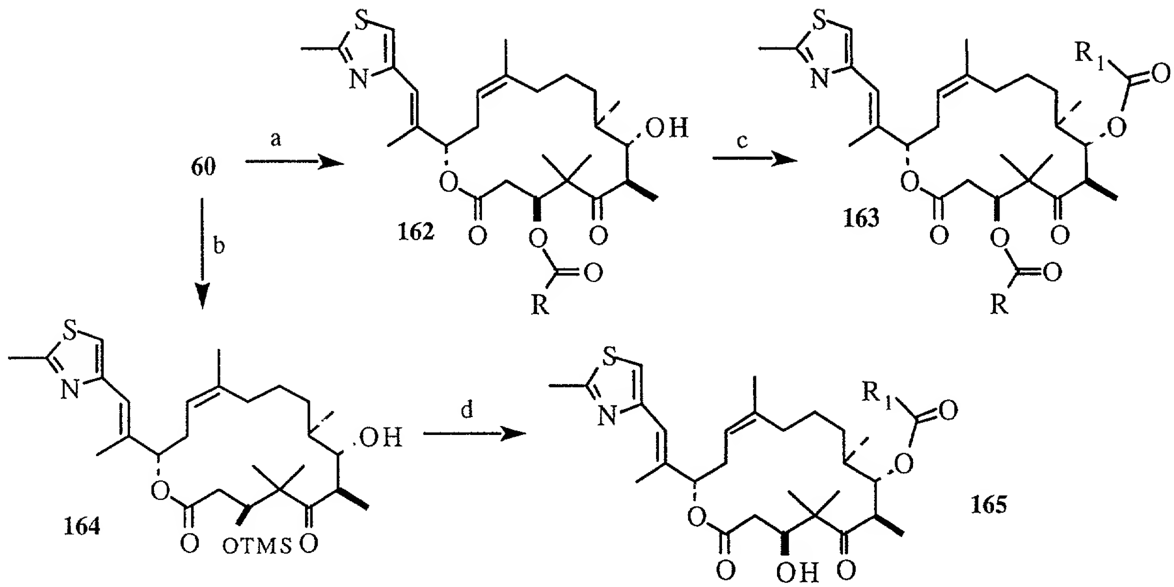


FIG. 26b



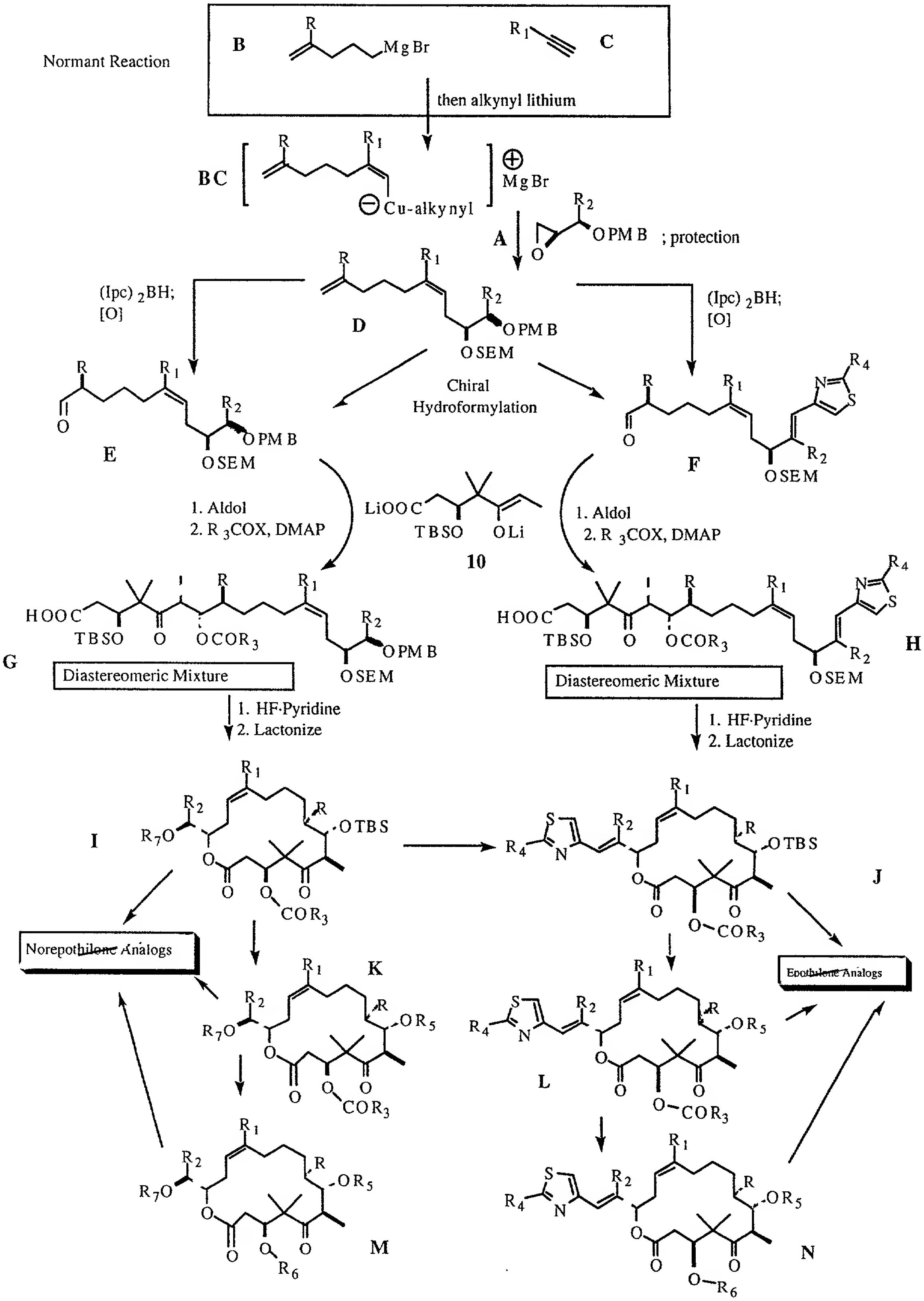
Key: a) Mg, ether; then propyne, Cu(I); pentynyl lithium; epoxide **143** (Scheme XXIII); then H_3O^+; b) β-lactone **157** (Scheme XXIII), pyridine, CH_2Cl_2; c) Mg, ether; then propyne, Cu(I); pentynyl lithium; β-lactone **157** (Scheme XXIII); then p-$MeOC_6H_4CH_2OCH_2Cl$ or other protecting group such as TBSOTf or TBSCl; d) $(Ipc)_2BH$, THF; then LiOOH; e) Swern Oxidation; f) $(Ipc)_2BH$, THF; then PCC; g) Lewis or protic acid; or alternatively base catalyzed cyclization; h) DDQ, CH_2Cl_2, HOH, buffer to remove the PMB, PMBM or DMB groups; Fluoride ion to remove Si based groups.

FIG. 27



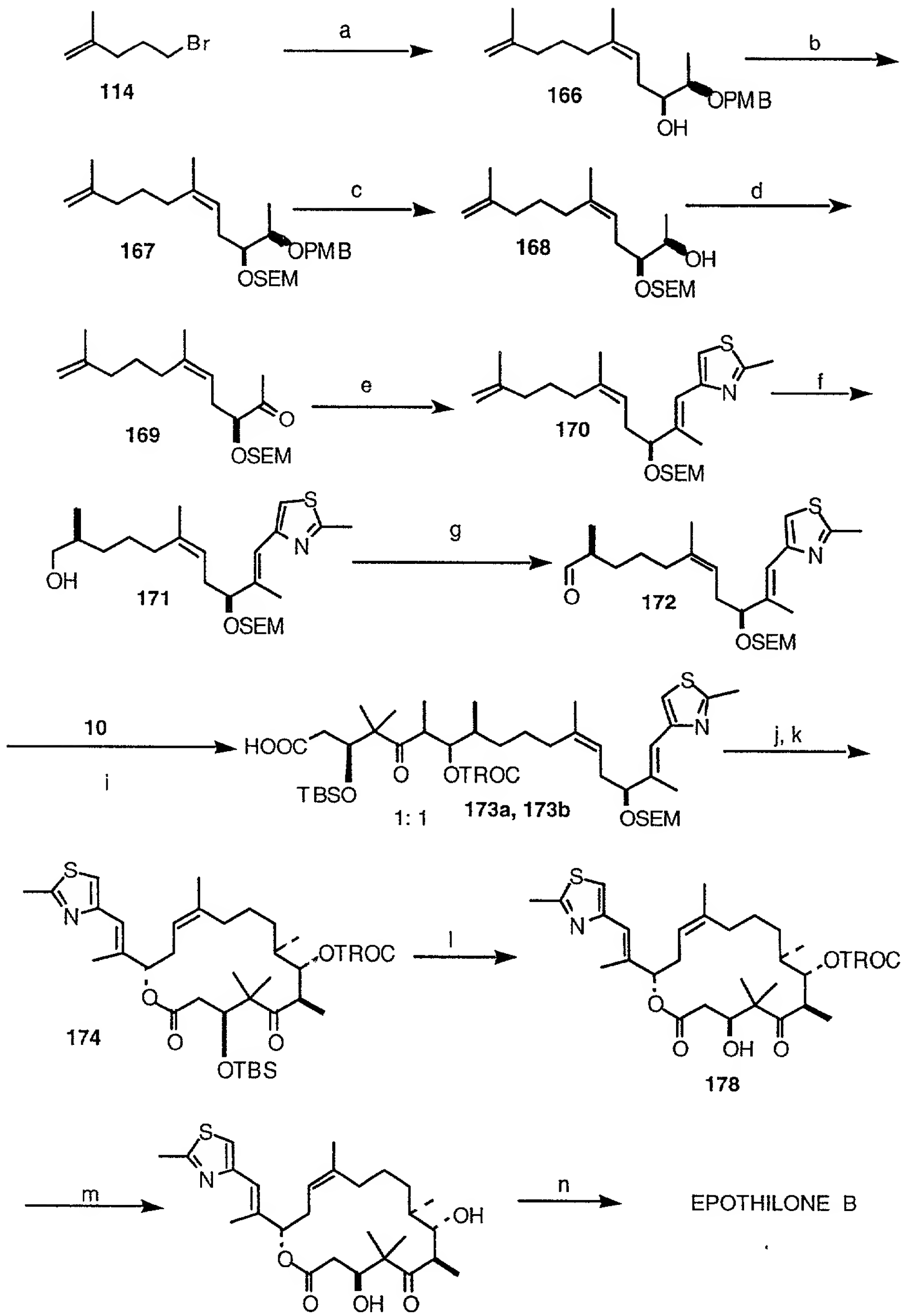
Key: a) RCOX, pyridine, catalytic DMAP, CH_2Cl_2; b) TMSOTf, 2,6-lutidine, CH_2Cl_2; c) R1COX, DMAP, CH_2Cl_2; d) R1COX, DMAP, CH_2Cl_2; then silica gel. Where RCOX = active ester of usual variety.

FIG. 28



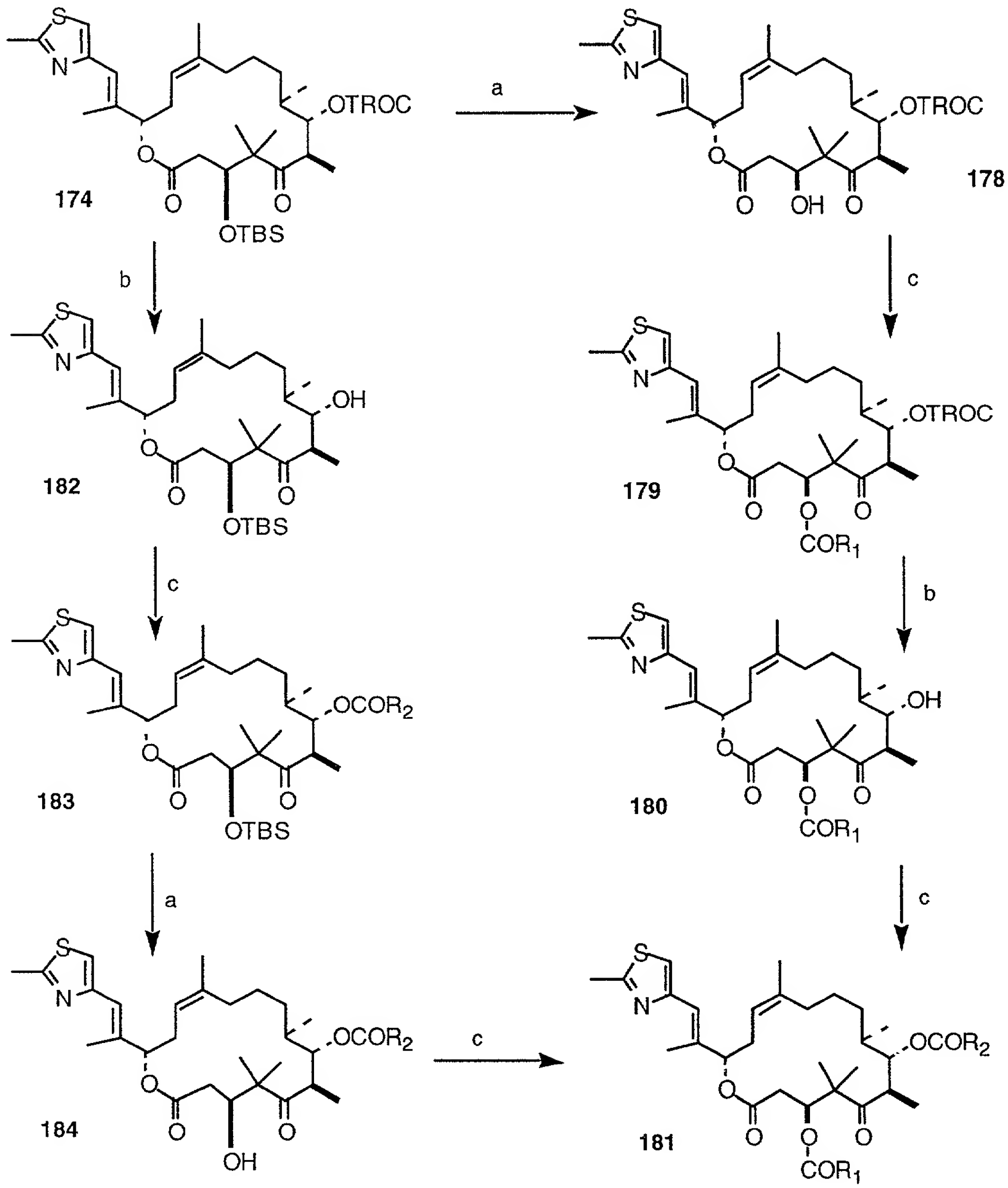
Normant Reaction
B
C
then alkynyl lithium
BC
Cu-alkynyl
MgBr
A
; protection
D
(Ipc) 2BH;
[O]
Chiral
Hydroformylation
E
F
1. Aldol
2. R 3COX, DMAP
LiOOC
TBSO
OLi
10
G
H
Diastereomeric Mixture
1. HF·Pyridine
2. Lactonize
I
J
K
L
M
N
Norepothilone Analogs
Epothilone Analogs

FIG. 29



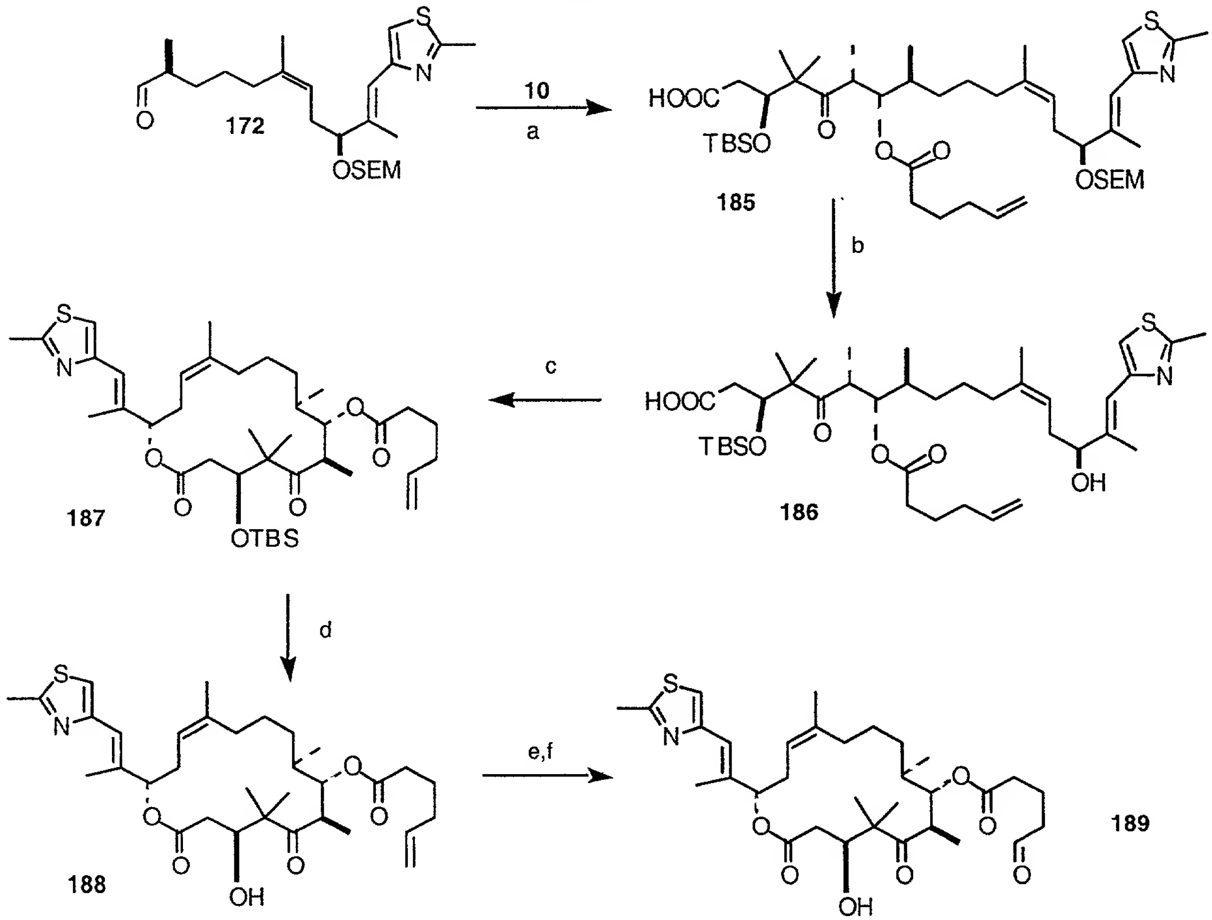
Key: a) i. Mg, ether; ii. CuBr•DMS complex, ether, DMS, -45°C; iii. propyne, -23°C; iv. Li-hexyne, HMPA, -78°C; v. **5c**, -78°C to -25°C, 78%; b) SEM-Cl, DIPEA, CH_2Cl_2, 94%; c) DDQ, CH_2Cl_2, HOH; 85%; d) SO_3•pyr, TEA, CH_2Cl_2; 78%; e) **24**, n-BuLi, THF, -78°C to R.T., 85%; f) $(Ipc)_2BH$, THF; H_2O_2, 82%; g) oxalyl chloride, DMSO, TEA, CH_2Cl_2, 88%; h) LDA, -78°C to -40°C, $ZnCl_2$; -78°C to -50°C, THF, 68%; i) TROC-Cl, DMAP, CH_2Cl_2, j) TFA, CH_2Cl_2, k) Trichlorobenzoyl chloride, TEA, THF, DMAP, toluene; l) HF•pyridine; m) Zn, HOAc; n) m-CPBA, CH_2Cl_2.

FIG. 30



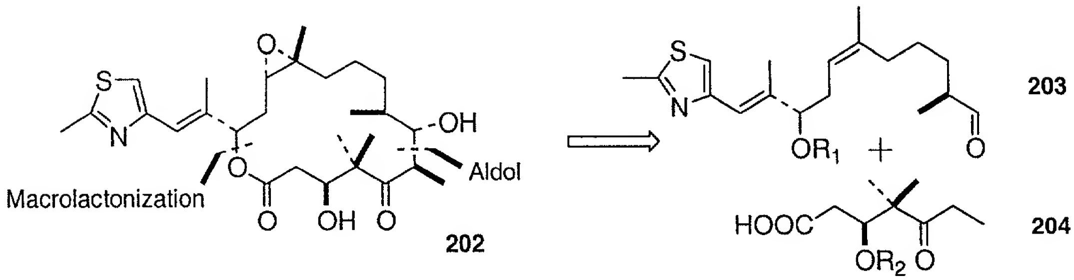
Key: a) HF•pyridine, THF; b) Zn, HOAc; c) RCOOH, DCC, TEA, DCM.

FIG. 31



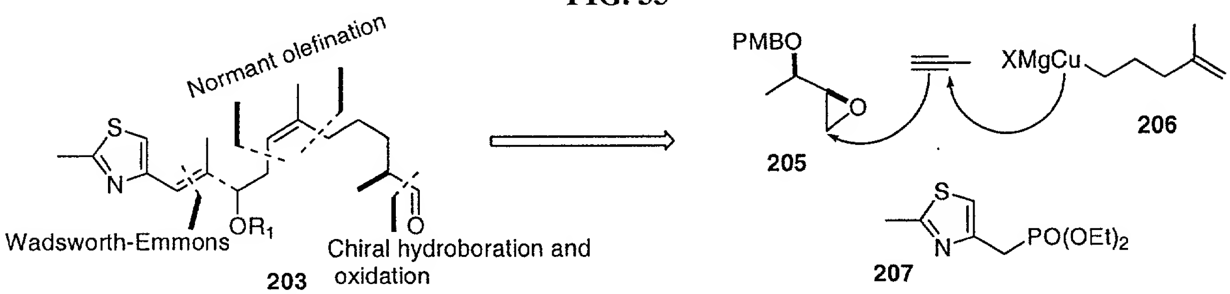
Key: a) LDA, -78°C to -40°C, $ZnCl_2$; -78°C to -50°C, THF, 68%; then $CH_2=CH(CH_2)_3COCl$, DMAP, CH_2Cl_2, b) TFA, CH_2Cl_2, c) Trichlorobenzoyl chloride, TEA, THF, DMAP, toluene; d) HF•pyridine; e) vicinal dihydroxylation; f) $NaIO_4$, THF, HOH.

FIG. 32



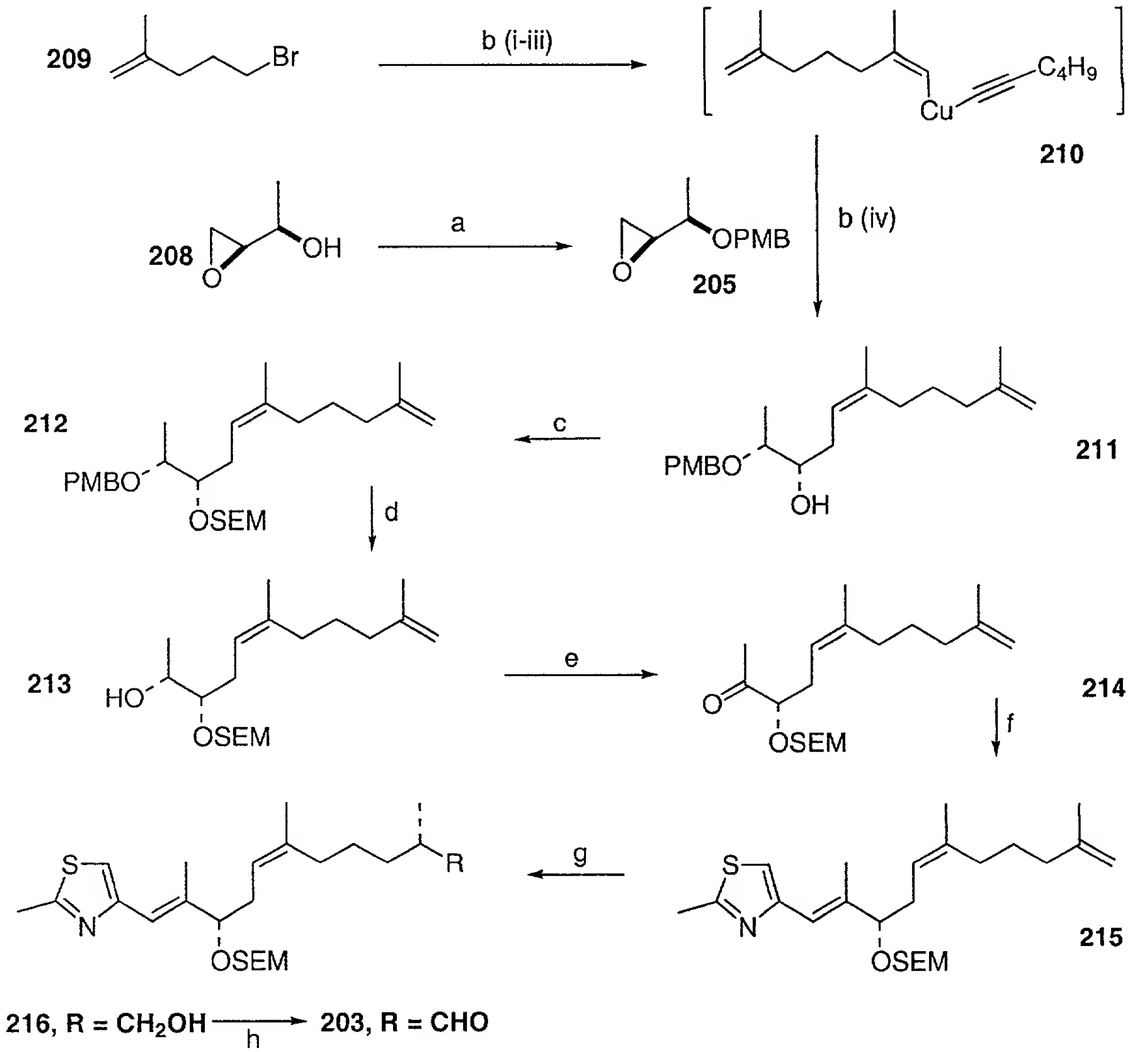
Macrolactonization
Aldol
202
203
204
OR$_1$
OR$_2$
HOOC

FIG. 33



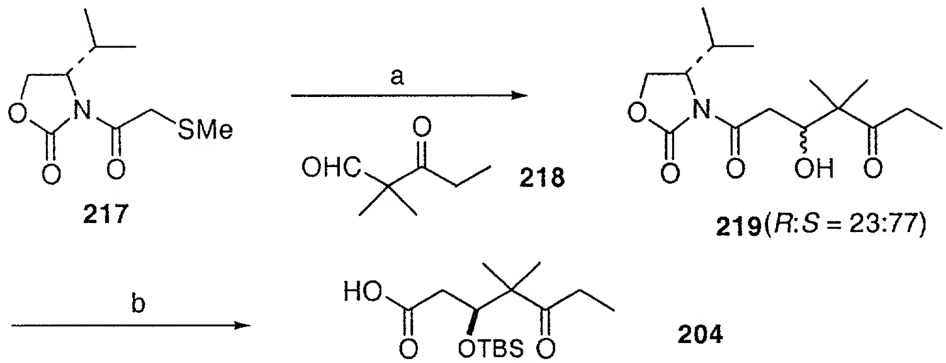
Normant olefination
Wadsworth-Emmons
OR$_1$
Chiral hydroboration and oxidation
203
PMBO
XMgCu
205
206
207
PO(OEt)$_2$

FIG. 34



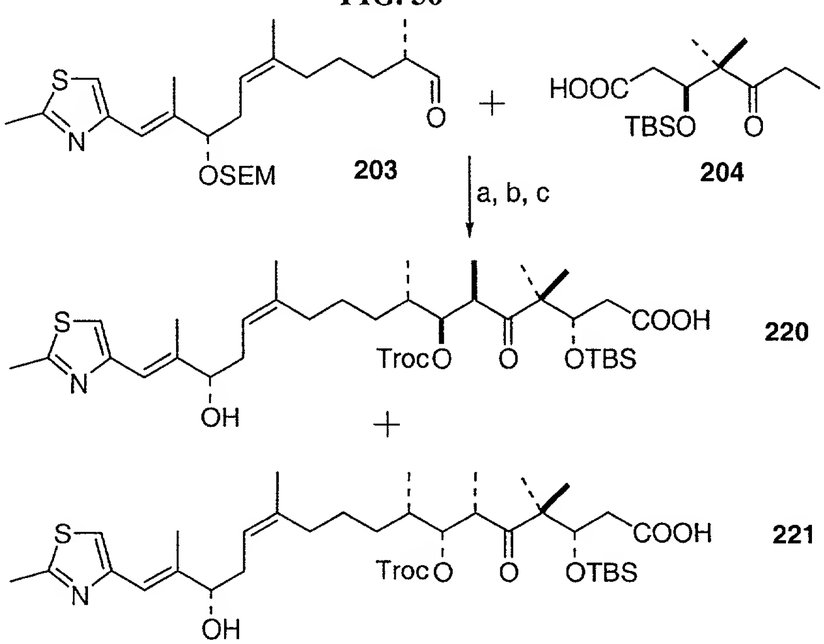
Key: a) PMB-Br,NaH, Bu_4N-I, THF, 0 °C, 85%; b) i) Mg, ether, rt; ii) CuBr-DMS, ether, DMS, -45°C, 3h, iii) Propyne, -45 °C to -23 °C, 4h then lithiohexyne, -78°C, 1h; iv) epoxide **205**, -78 °C, 1h, -25 °C, 24h, 76%; c) SEMCl, DIPEA, DCM, 0°C, 92%; d) DDQ, DCM:water (8:2), 88%; e) DMSO, $(COCl)_2$, DCM, TEA, -78 °C, 85%; f) **207**, *n*-BuLi, THF, then **214**, 72%; g) (*i*-PC)$_2$BH, THF, 0.5h, aq. $NaBO_3$; and h) DMSO, $(COCl)_2$, DCM, TEA, -78 °C, 92%.

FIG. 35



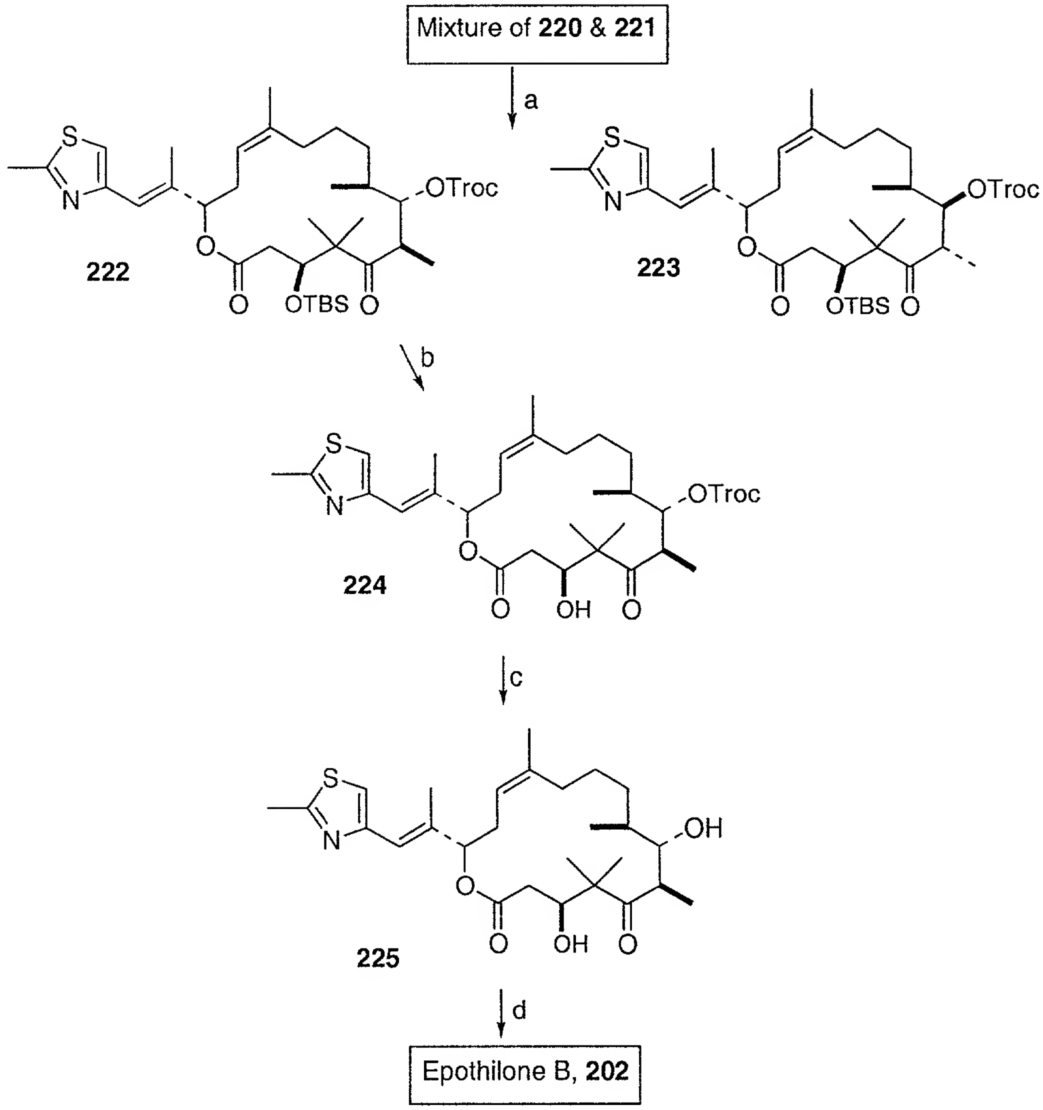
Key: (a) (i) Bu_2BOTf, DIPEA, CH_2Cl_2, 0 ^{0}C then add **217** at -78 ^{0}C; (ii) Raney Ni, acetone, 60 ^{0}C, 45 min, 70% combined; (b) (i) TBDMSOTf, 2,6-lutidine, CH_2Cl_2, 0 ^{0}C to rt, 95%; (ii) LiOH, H_2O_2, THF-H_2O, rt, 82%.

FIG. 36



Key: a) LDA, **204**, THF, -78 ^{0}C to -40 ^{0}C then to -78 ^{0}C, $ZnCl_2$, **203**, -78 ^{0}C to -50 ^{0}C, 0.5h; b) TrocCl, Py, DCM, 0 ^{0}C; c) TFA, DCM (3:7), -20 ^{0}C, 1h, 63% (three steps).

FIG. 37



Key: (a) 2,4,6-$Cl_3C_6H_2COCl$, TEA, THF, DMAP, toluene, rt, 1h; b) HF-Py, DCM, rt, 95%; c) Zn, aq. NH_4Cl, MeOH, reflux, 92%; d) [Methyl(trifluoromethyl)]dioxirane, MeCN, 0 ^{o}C, 56%.